PA..NT COOPERATION TREAT

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

TAIT, Brian, Steele
AstraZeneca
Global Intellectual Property
P.O. Box 272
Mereside, Alderley Park
Macclesfield, Cheshire SK10 4GR
ROYAUME-UNI

Date of mailing (day/month/year) 18 January 2002 (18.01.02)	
Applicant's or agent's file reference PHM.70569/WO	**IMPORTANT NOTIFICATION**
International application No. PCT/GB00/02566	**International filing date** (day/month/year) 04 July 2000 (04.07.00)

1. The following indications appeared on record concerning:

[X] the applicant [ ] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
ASTRAZENECA SA Le Galien 1, rue des Chauffours Boite postale 127 F-95022 Cergy Cedex France	GB	GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
DELETED.		
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Ki-Nam HA
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/306 (March 1994)

004602369

PA .NT COOPERATION TREAT.

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

TAIT, Brian, Steele
AstraZeneca
Global Intellectual Property
P.O. Box 272
Mereside, Alderley Park
Macclesfield, Cheshire SK10 4GR
ROYAUME-UNI

Date of mailing (day/month/year)
28 November 2001 (28.11.01)

Applicant's or agent's file reference
PHM.70569/WO

IMPORTANT NOTIFICATION

International application No.
PCT/GB00/02566

International filing date (day/month/year)
04 July 2000 (04.07.00)

1. The following indications appeared on record concerning:

[X] the applicant [ ] the inventor [ ] the agent [ ] the common representative

Name and Address
ASTRAZENECA SA
Le Galien
1, rue des Chauffours
Boite postale 127
F-95022 Cergy Cedex
France

State of Nationality: GB
State of Residence: GB
Telephone No.:
Facsimile No.:
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address
DELETED

State of Nationality:
State of Residence:
Telephone No.:
Facsimile No.:
Teleprinter No.:

3. Further observations, if necessary:
Sole applicant for all designated States except US is now : ASTRAZENECA UK LIMITED.

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
R. Raissi

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 14 March 2001 (14.03.01)	
International application No. PCT/GB00/02566	**Applicant's or agent's file reference** PHM.70569/WO
International filing date (day/month/year) 04 July 2000 (04.07.00)	**Priority date** (day/month/year) 07 July 1999 (07.07.99)
Applicant CRAWLEY, Graham, Charles et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

23 January 2001 (23.01.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Juan Cruz
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date 10/019745

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* PHM.70569/WO

Box No. I TITLE OF INVENTION

QUINAZOLINE DERIVATIVES

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

ASTRAZENECA UK LIMITED
15 Stanhope Gate
London
W1Y 6LN
GB

☐ This person is also inventor.

Telephone No.
(01625) 516485

Facsimile No.
(01625) 583358

Teleprinter No.
669095/669388

State *(that is, country)* of nationality:
GB

State *(that is, country)* of residence:
GB

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

ZENECA PHARMA S.A.
'Le Galien'
1 rue des Chauffours, BP127
95022 Cergy Cedex
FR

This person is:
☒ applicant only
☐ applicant and inventor
☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:
GB

State *(that is, country)* of residence:
GB

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

TAIT, Brian Steele et al
ASTRAZENECA
Global Intellectual Property
P O Box 272
Mereside, Alderley Park
Macclesfield, Cheshire, SK10 4GR
GB

Telephone No.
(01625) 514151

Facsimile No.
(01625) 583358

Teleprinter No.
669095/669388

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

CRAWLEY, Graham Charles
Alderley Park
Macclesfield
Cheshire
SK10 4TG
GB

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: GB

State *(that is, country)* of residence: GB

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

MCKERRECHER, Darren
Alderley Park
Macclesfield
Cheshire
SK10 4TG
GB

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: GB

State *(that is, country)* of residence: GB

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

POYSER, Jeffrey Philip
Alderley Park
Macclesfield
Cheshire
SK10 4TG
GB

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: GB

State *(that is, country)* of residence: GB

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

HENNEQUIN, Laurent Francois Andre
Z.I. La Pompelle
BP 1050
51689 Reims Cedex 2
FR

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: FR

State *(that is, country)* of residence: FR

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

PLE, Patrick
Z.I. La Pompelle
BP 1050
51689 Reims Cedex 2
FR

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: FR

State *(that is, country)* of residence: FR

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

LAMBERT, Christine Marie Paul
Z.I. La Pompelle
BP 1050
51689 Reims Cedex 2
FR

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: BE

State *(that is, country)* of residence: FR

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☐ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☐ the United States of America only
- ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No. V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*:

Regional Patent

- [X] **AP** **ARIPO Patent:** **GH** Ghana, **GM** Gambia, **KE** Kenya, **LS** Lesotho, **MW** Malawi, **SD** Sudan, **SL** Sierra Leone, **SZ** Swaziland, **TZ** United Republic of Tanzania, **UG** Uganda, **ZW** Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- [X] **EA** **Eurasian Patent:** **AM** Armenia, **AZ** Azerbaijan, **BY** Belarus, **KG** Kyrgyzstan, **KZ** Kazakhstan, **MD** Republic of Moldova, **RU** Russian Federation, **TJ** Tajikistan, **TM** Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- [X] **EP** **European Patent:** **AT** Austria, **BE** Belgium, **CH and LI** Switzerland and Liechtenstein, **CY** Cyprus, **DE** Germany, **DK** Denmark, **ES** Spain, **FI** Finland, **FR** France, **GB** United Kingdom, **GR** Greece, **IE** Ireland, **IT** Italy, **LU** Luxembourg, **MC** Monaco, **NL** Netherlands, **PT** Portugal, **SE** Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- [X] **OA** **OAPI Patent:** **BF** Burkina Faso, **BJ** Benin, **CF** Central African Republic, **CG** Congo, **CI** Côte d'Ivoire, **CM** Cameroon, **GA** Gabon, **GN** Guinea, **GW** Guinea-Bissau, **ML** Mali, **MR** Mauritania, **NE** Niger, **SN** Senegal, **TD** Chad, **TG** Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

- [X] **AE** United Arab Emirates
- [X] **AL** Albania
- [X] **AM** Armenia
- [X] **AT** Austria
- [X] **AU** Australia
- [X] **AZ** Azerbaijan
- [X] **BA** Bosnia and Herzegovina
- [X] **BB** Barbados
- [X] **BG** Bulgaria
- [X] **BR** Brazil
- [X] **BY** Belarus
- [X] **CA** Canada
- [X] **CH and LI** Switzerland and Liechtenstein
- [X] **CN** China
- [X] **CR** Costa Rica
- [X] **CU** Cuba
- [X] **CZ** Czech Republic
- [X] **DE** Germany
- [X] **DK** Denmark
- [X] **DM** Dominica
- [X] **EE** Estonia
- [X] **ES** Spain
- [X] **FI** Finland
- [X] **GB** United Kingdom
- [X] **GD** Grenada
- [X] **GE** Georgia
- [X] **GH** Ghana
- [X] **GM** Gambia
- [X] **HR** Croatia
- [X] **HU** Hungary
- [X] **ID** Indonesia
- [X] **IL** Israel
- [X] **IN** India
- [X] **IS** Iceland
- [X] **JP** Japan
- [X] **KE** Kenya
- [X] **KG** Kyrgyzstan
- [X] **KP** Democratic People's Republic of Korea
- [X] **KR** Republic of Korea
- [X] **KZ** Kazakhstan
- [X] **LC** Saint Lucia
- [X] **LK** Sri Lanka
- [X] **LR** Liberia
- [X] **LS** Lesotho
- [X] **LT** Lithuania
- [X] **LU** Luxembourg
- [X] **LV** Latvia
- [X] **MA** Morocco
- [X] **MD** Republic of Moldova
- [X] **MG** Madagascar
- [X] **MK** The former Yugoslav Republic of Macedonia
- [X] **MN** Mongolia
- [X] **MW** Malawi
- [X] **MX** Mexico
- [X] **NO** Norway
- [X] **NZ** New Zealand
- [X] **PL** Poland
- [X] **PT** Portugal
- [X] **RO** Romania
- [X] **RU** Russian Federation
- [X] **SD** Sudan
- [X] **SE** Sweden
- [X] **SG** Singapore
- [X] **SI** Slovenia
- [X] **SK** Slovakia
- [X] **SL** Sierra Leone
- [X] **TJ** Tajikistan
- [X] **TM** Turkmenistan
- [X] **TR** Turkey
- [X] **TT** Trinidad and Tobago
- [X] **TZ** United Republic of Tanzania
- [X] **UA** Ukraine
- [X] **UG** Uganda
- [X] **US** United States of America
- [X] **UZ** Uzbekistan
- [X] **VN** Viet Nam
- [X] **YU** Yugoslavia
- [X] **ZA** South Africa
- [X] **ZW** Zimbabwe

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

- [X] DZ Algeria
- [X] AG Antigua

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 07 JULY 1999 (07/07/99)	99401692.1	EP		
item (2) 04 MAY 2000 (04/05/2000)	00401221.7	EP		
item (3)				

☐ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): _____

* *Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used)* :

ISA / EPO

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority)*:

Date *(day/month/year)* Number Country *(or regional Office)*

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following **number of sheets**:

request	: 5
description (excluding sequence listing part)	: 147
claims	: 15
abstract	: 1
drawings	:
sequence listing part of description	:
Total number of sheets	: 168

This international application is **accompanied** by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s): (1)
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☐ other *(specify)*:

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: ENGLISH

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Brian S. Tait.

TAIT, Brian Steele et al.

For receiving Office use only

1. Date of actual receipt of the purported international application:
2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority (if two or more are competent): ISA /
6. ☐ Transmittal of search copy delayed until search fee is paid.

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/02566

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D239/94 A61K31/505 C07D401/12 C07D403/12 C07D495/04
A61P37/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 50047 A (UNIV PENNSYLVANIA ;LIANG BRUCE T (US); JACOBSON KENNETH A (US)) 12 November 1998 (1998-11-12) see compound MRS1364 page 28 ---	1,4,13, 14
X	WO 98 50370 A (KUTSCHER BERNHARD ;WEINBERGER HEINZ (DE); SUGEN INC (US); TANG PEN) 12 November 1998 (1998-11-12) cited in the application see compounds A32-A34 page 53, line 5 -page 55, line 9 ---	15,16
X	WO 98 38984 A (SUGEN INC ;SHENOY NARMADA (US); WAGNER GREGORY S (US)) 11 September 1998 (1998-09-11) page 28, line 22 -page 29, line 8 page 76, line 3-24 ---	15,16

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 October 2000	26.10.00

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Schmid, J-C

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inter ional Application No
PCT/GB 00/02566

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 09024 A (JOHNS AMANDA ;PORTER RODERICK ALAN (GB); SMITHKLINE BEECHAM PLC (G) 25 February 1999 (1999-02-25) cited in the application page 1, line 34 -page 2, line 31 see formula (I) page 3, line 26 -page 4, line 28	1,2, 14-16
A	WO 97 03069 A (GLAXO GROUP LTD ;COCKERILL GEORGE STUART (GB); CARTER MALCOLM CLIV) 30 January 1997 (1997-01-30) cited in the application page 1, line 1 -page 2, line 3 see formula(I) page 7, line 1 -page 9, line 10	1-16
A	MYERS M R ET AL: "The preparation and SAR of 4-(anilino), 4-(phenoxy), and 4-(thiophenoxy)-quinazolines: inhibitors of p56and EGF-R tyrosine kinase activity" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS,GB,OXFORD, vol. 7, no. 4, 18 February 1997 (1997-02-18), pages 417-420, XP004136037 ISSN: 0960-894X the whole document	1-16
A	GIBSON K H ET AL: "Epidermal growth factor receptor tyrosine kinase: structure-activity relationships and antitumour activity of novel quinazolines" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS,GB,OXFORD, vol. 7, no. 21, 4 November 1997 (1997-11-04), pages 2723-2728, XP004136520 ISSN: 0960-894X cited in the application see compound 18	1-16
A	HONG C I ET AL: "SYNTHESIS AND BIOLOGICAL ACTIVITIES OF SOME N4-SUBSTITUTED 4-AMINOPYRAZOLO'3,4d!PYRIMIDINES" JOURNAL OF MEDICINAL CHEMISTRY,AMERICAN CHEMICAL SOCIETY. WASHINGTON,US, vol. 19, no. 4, 1976, pages 555-558, XP000916640 ISSN: 0022-2623 cited in the application see compounds 20,22-26	1-16

-/—

INTERNATIONAL SEARCH REPORT

Intern bnal Application No
PCT/GB 00/02566

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	VAN MUIJLWIJK-KOEZEN ET AL: "Isoquinoline and Quinazoline Urea Analogues as Antagonists for the Human Adenosine A3 Receptor" JOURNAL OF MEDICINAL CHEMISTRY,AMERICAN CHEMICAL SOCIETY. WASHINGTON,US, vol. 43, no. 5, 1 June 2000 (2000-06-01), pages 2227-2238, XP002147879 ISSN: 0022-2623 see compound 5a	1,2, 14-16

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Intl. tional application No.
PCT/GB 00/02566

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 16 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.

2. [X] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claim 1 relates to an extremely large number of possible compounds. In fact, the claims contain so many options that a lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear, namely for those quinazoline derivatives of claim 1 for which Q1 is a group of formula Ia, Ib, Ic or Id.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interr pnal Application No
PCT/GB 00/02566

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9850047 A	12-11-1998	AU 7367798 A	27-11-1998
		EP 0991414 A	12-04-2000
WO 9850370 A	12-11-1998	AU 7282998 A	27-11-1998
		EP 0981519 A	01-03-2000
WO 9838984 A	11-09-1998	AU 6680698 A	22-09-1998
		EP 1014953 A	05-07-2000
WO 9909024 A	25-02-1999	AU 8741198 A	08-03-1999
		EP 1003737 A	31-05-2000
WO 9703069 A	30-01-1997	AU 6613996 A	10-02-1997
		EP 0843671 A	27-05-1998
		HR 960316 A	28-02-1998
		JP 11508906 T	03-08-1999

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PHM.70569/WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02566	04/07/2000	07/07/1999

International Patent Classification (IPC) or national classification and IPC
C07D239/94

Applicant
ASTRAZENECA UK LIMITED et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23/01/2001	11.10.2001

Name and mailing address of the international preliminary examining authority:

European Patent Office
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Authorized officer

Schmid, J-C

Telephone No. +49 89 2399 8347

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02566

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-147	as originally filed				
Claims, No.:					
1 (part),2,3,6-14, 15 (part)	as originally filed				
1 (part),4,5,15 (part), 16	as received on	13/06/2001	with letter of	07/06/2001	

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 1(part).

because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

   ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 1(part).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 3-12
	No:	Claims 1,2,13-16
Inventive step (IS)	Yes:	Claims 6-12

	No:	Claims	1-5, 13-16
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

SECTION III

Claim 16 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

SECTION V

Reference is made to the following documents:

D1: WO 98 50047 A (UNIV PENNSYLVANIA ;LIANG BRUCE T (US); JACOBSON KENNETH A (US)) 12 November 1998 (1998-11-12)

D2: WO 98 50370 A (KUTSCHER BERNHARD ;WEINBERGER HEINZ (DE); SUGEN INC (US); TANG PEN) 12 November 1998 (1998-11-12) cited in the application

D3: WO 98 38984 A (SUGEN INC ;SHENOY NARMADA (US); WAGNER GREGORY S (US)) 11 September 1998 (1998-09-11)

D4: WO 99 09024 A (JOHNS AMANDA ;PORTER RODERICK ALAN (GB); SMITHKLINE BEECHAM PLC (G) 25 February 1999 (1999-02-25) cited in the application

D5: WO 97 03069 A (GLAXO GROUP LTD ;COCKERILL GEORGE STUART (GB); CARTER MALCOLM CLIV) 30 January 1997 (1997-01-30) cited in the application

D6: MYERS M R ET AL: 'The preparation and SAR of 4-(anilino), 4-(phenoxy), and 4-(thiophenoxy)-quinazolines: inhibitors of p56and EGF-R tyrosine kinase activity' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS,GB,OXFORD, vol. 7, no. 4, 18 February 1997 (1997-02-18), pages 417-420, XP004136037 ISSN: 0960-894X

D7: GIBSON K H ET AL: 'Epidermal growth factor receptor tyrosine kinase: structure-activity relationships and antitumour activity of novel quinazolines' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS,GB,OXFORD, vol. 7, no. 21, 4 November 1997 (1997-11-04), pages 2723-2728, XP004136520 ISSN: 0960-894X cited in the application

D8: HONG C I ET AL: 'SYNTHESIS AND BIOLOGICAL ACTIVITIES OF SOME N4-SUBSTITUTED 4-AMINOPYRAZOLO[3,4d]PYRIMIDINES' JOURNAL OF MEDICINAL CHEMISTRY,AMERICAN CHEMICAL SOCIETY. WASHINGTON,US, vol. 19, no. 4, 1976, pages 555-558, XP000916640 ISSN: 0022-2623 cited in the application

D9: VAN MUIJLWIJK-KOEZEN ET AL: 'Isoquinoline and Quinazoline Urea Analogues as Antagonists for the Human Adenosine A3 Receptor' JOURNAL OF MEDICINAL CHEMISTRY,AMERICAN CHEMICAL SOCIETY. WASHINGTON,US, vol. 43, no. 5, 1 June 2000 (2000-06-01), pages 2227- 2238, XP002147879 ISSN: 0022-2623

1). D2 and D3 disclose three compounds that have been disclaimed in claims 1 to 14. However, the compounds have been disclosed in D2 and D3 for some of the claimed uses (autoimmune disease, psoriasis, arthritis... -see D2, page 33, line 13; D3, page 29, line 9). The fact that these prior art compounds have been disclosed to act against those diseases by another mechanism of action cannot restore novelty.

D2 and D3 are therefore novelty-destroying for claims 15 and 16.

The compounds of present claims 1 and 2 generically overlap with the compounds of formula (I) of D4.

The overlap concerns the compounds of D4 wherein X and Y represent N.

This overlap is considered to be novelty-destroying for present claim 1 since a selection from known subject-matter to be novel must fulfil the requirement that the selection portion is small and that a technical rule of selection has been applied, so that a technical teaching results which is different from that of the state of the art.

In the Examer's judgment a true selection from a broader technical disclosure to be novel must add a new element to the state of the art. The mere selection of one from three alternatives disclosed in a document belonging to the state of the art is no more than a repetition of what already belongs to the state of the art and cannot, therefore, be novel.

Either the whole overlap has to be removed by the mean of a proviso or the novelty should be restored by the mean of positive features which provide a technical rule of selection.

The subject-matter of claims 6 to 9 is regarded as a novel selection over the overlap with the compounds generically disclosed in D4 on account of the combination of selection of the nucleus (Y = N) with the substitution in specific positions.

Accordingly, the subject-matter of claim 1, 2 and 14 to 16 lacks novelty over D2-D4 (Article 33(2) PCT).

Compound MRS 1364 disclosed on page 28 of D1 has been excluded from the claimed scope by means of disclaimer. The claimed-matter is therefore novel over D1.

D5 and D6 disclose no urea derivatives (see the meaning of Yand X for the compounds disclosed respectively in D5 and D6).

D7 discloses the 1-(6,7-dimethoxyquinazolin-4-yl)-3-phenylurea (compound 18) which is excluded from the scope of product-claims 1 to 14. This compound is inactive as an EGF RTK inhibitor.

D8 disclosed some pyrazolo[3,4-d]pyrimidine derivative which are excluded from the scope of claim 1 to 14 by means of the provisos.

The compounds of D8 are disclosed as inhibitors of L1210 leukemia and human leukemic myeloblasts.

Accordingly, the subject-matter of claims 1 to 16 is novel over D1 and D5-D8 (Article 33(2) PCT.

2). The technical problem underlying the application is the provision of compounds which selectively inhibit enzyme $p56^{lck}$ tyrosine kinase (see present description on page 3, lines 4-11).

Tyrosine kinase inhibitors have been disclosed in D5. However, these compounds are not selective inhibitors of $p56^{lck}$ tyrosine kinase (see table 1 and 2 of D5).

The closest prior art is therefore seen in D6 which discloses a selective $p56^{lck}$ tyrosine kinase inhibitor (see compound 10).

It was not obvious in the light of D6, also taken in combination with the teaching of D5, that the replacement of the NH, O or S link of the quinazoline derivatives by an urea or thiourea would result in a selective $p56^{lck}$ tyrosine kinase inhibitority activity of the resulting compounds.

An inventive step can therefore be acknowledged for those present compounds which effectively solve the above-mentioned technical problem, i.e for the present working examples 1-34 and the for the obvious equivalents thereof which can be represented by those of claims 6 to 12. The Applicant confirmed that about 250 compounds disclosed in examples 1-34 of the application have been have found to possess (valuable) $p56^{lck}$ tyrosine kinase inhibitority activity (IC_{50} comprised within the range of 0.0001-5 µM). However, the selectivity of this inhibitory activity has still not been confirmed.

It must furthermore be noted that the breadth of the claims should be such that it represents a reasonable generalisation over the examples provided, and such that substantially all compounds falling within their scope actually are solutions to the technical problem underlying the invention (Article 33(3) EPC).

In this respect it must be noted that most of the compounds claimed in claims 1 to 5 cannot be regarded as obvious modifications or equivalents of the examples which have been given in the description if the specificity of the technical problem underlying the application is taken into account. Examination of the examples indicates that there are no working examples with compounds of formula V, one working example for those of formula III (example 18). It is pointed out that all the quinazoline and quinoline derivatives derivative of the working example are substituted in positions 6 and/or 7 by an optionally substituted alkoxy group. This very few variations of the substituents R^1 cannot support the broad generalisation made in claims 1 to 5.
Still with respect to the breath of the claims, it must be noted that expressions in the claims, such as "aryl", "heteroaryl", "heterocyclyc"..., are non-limitative in scope and therefore cannot be regarded as obvious modifications or equivalents of the examples which have been given in the description. Accordingly, the said expressions should be restricted in this respect to the particular meanings specified in the general part of description which can be regarded as obvious equivalents over the tested compounds.

It must further be noticed that the inventive step has been acknowledged for a structural difference which must be regarded rather as minor, when the generalisation made by the Applicant in the claim is considered.
The examiner is therefore not satisfied that substantially all the compounds of the formula (I) with the substituents as recited claims 1 to 5 are selective $p56^{lck}$ tyrosine kinase inhibitors.
Consequently, at the present stage of the examining procedure, for claims 1 to 5, the technical problem underlying the application must be reformulated into the provision of further organic compounds.
As there is no technical prejudice for the preparation of the claimed compounds, no inventive step can be acknowledged for the whole subject-matter of claims 1 to

5 due to the compounds encompassed by these claims which are likely not selective $p56^{lck}$ tyrosine kinase inhibitority
Accordingly, claims 1 to 5 do not meet the requirement of Article 33(3) PCT.

SECTION VI

D9 was published between the priority and filing dates of the present application. No check has been made as to whether the priority of the present application has been validly claimed.

halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulphinyl, (1-6C)alkylsulphonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulphamoyl, N,N-di-[(1-6C)alkyl]sulphamoyl, (1-6C)alkanesulphonylamino and N-(1-6C)alkyl-(1-6C)alkanesulphonylamino, or from a group of the formula :

$$-X^8-R^{15}$$

wherein X^8 is a direct bond or is selected from O and $N(R^{16})$, wherein R^{16} is hydrogen or (1-6C)alkyl, and R^{15} is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl or di-[(1-6C)alkyl]amino-(1-6C)alkyl,

and wherein any heterocyclyl group within a substituent on Q^2 optionally bears 1 or 2 oxo or thioxo substituents;

or a pharmaceutically-acceptable salt thereof;

provided that the compounds :-

1-(6,7-dimethoxyquinazolin-4-yl)-3-phenylurea,

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-phenylurea,

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-bromophenyl)urea,

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-methoxyphenyl)urea.

1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

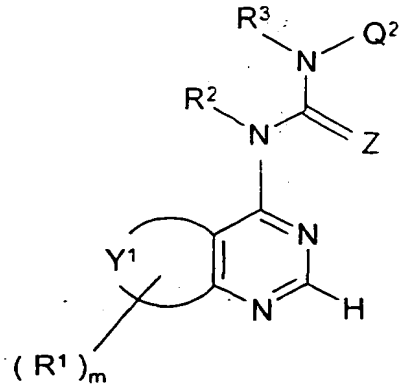
1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and

1-{8-[3,4-dihydroxy-5(N-ethylcarbamoyl)tetrahydrofuran-2-yl]-7,8-dihydropteridin-4-yl}-3-(4-nitrophenyl)urea are excluded.

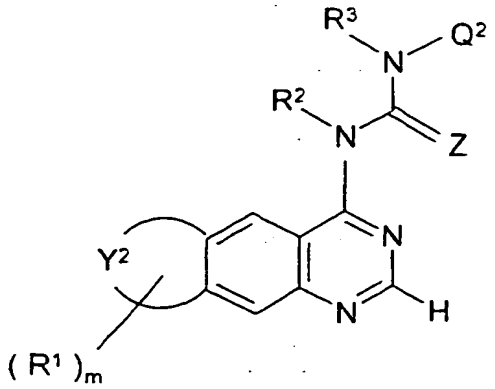
4. A pyrimidine derivative of the Formula IV



IV

wherein each of m, R^1, Y^1, R^2, R^3, Z and Q^2 has any of the meanings defined in claim 1;
or a pharmaceutically-acceptable salt thereof;
provided that the compounds :-
1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and
1-{8-[3,4-dihydroxy-5(N-ethylcarbamoyl)tetrahydrofuran-2-yl]-7,8-dihydropteridin-4-yl}-3-(4-nitrophenyl)urea are excluded.

5. A quinazoline derivative of the Formula V



V

wherein each of m, R^1, Y^2, R^2, R^3, Z and Q^2 has any of the meanings defined in claim 1;
or a pharmaceutically-acceptable salt thereof.

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-methoxyphenyl)urea.
1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and
1-{8-[3,4-dihydroxy-5(N-ethylcarbamoyl)tetrahydrofuran-2-yl]-7,8-dihydropteridin-4-yl}-3-(4-nitrophenyl)urea,
in the manufacture of a medicament for use in the prevention or treatment of T cell mediated diseases or medical conditions in a warm-blooded animal such as man.

16. A method for the prevention or treatment of T cell mediated diseases or medical conditions in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective amount of a quinazoline derivative of the Formula I, or a pharmaceutically-acceptable salt thereof, according to claim 1 but without the proviso that the group of formula Ic so formed is not a purine ring and including the compounds :-
1-(6,7-dimethoxyquinazolin-4-yl)-3-phenylurea,
1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-phenylurea,
1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-bromophenyl)urea,
1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-methoxyphenyl)urea.
1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and
1-{8-[3,4-dihydroxy-5(N-ethylcarbamoyl)tetrahydrofuran-2-yl]-7,8-dihydropteridin-4-yl}-3-(4-nitrophenyl)urea.

halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulphinyl, (1-6C)alkylsulphonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulphamoyl, N,N-di-[(1-6C)alkyl]sulphamoyl, (1-6C)alkanesulphonylamino and N-(1-6C)alkyl-(1-6C)alkanesulphonylamino, or from a group of the formula :

$$-X^8-R^{15}$$

wherein X^8 is a direct bond or is selected from O and $N(R^{16})$, wherein R^{16} is hydrogen or (1-6C)alkyl, and R^{15} is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl or di-[(1-6C)alkyl]amino-(1-6C)alkyl,

and wherein any heterocyclyl group within a substituent on Q^2 optionally bears 1 or 2 oxo or thioxo substituents;

or a pharmaceutically-acceptable salt thereof;

provided that the compounds :-

1-(6,7-dimethoxyquinazolin-4-yl)-3-phenylurea,

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-phenylurea,

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-bromophenyl)urea,

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-methoxyphenyl)urea.

1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

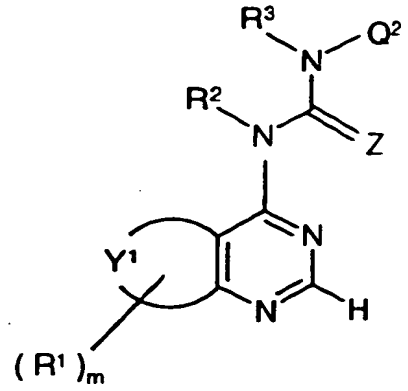
1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and

1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea are excluded.

4. A pyrimidine derivative of the Formula IV



IV

wherein each of m, R^1, Y^1, R^2, R^3, Z and Q^2 has any of the meanings defined in claim 1; or a pharmaceutically-acceptable salt thereof;

provided that the compounds :-

1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

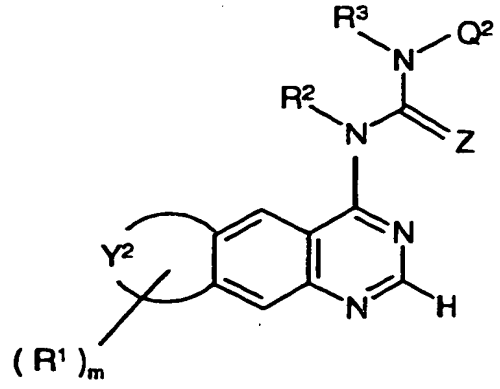
1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,

1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and

1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea are excluded.

5. A quinazoline derivative of the Formula V



V

wherein each of m, R^1, Y^2, R^2, R^3, Z and Q^2 has any of the meanings defined in claim 1; or a pharmaceutically-acceptable salt thereof.

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-methoxyphenyl)urea.
1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and
1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
in the manufacture of a medicament for use in the prevention or treatment of T cell mediated diseases or medical conditions in a warm-blooded animal such as man.

16. A method for the prevention or treatment of T cell mediated diseases or medical conditions in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective amount of a quinazoline derivative of the Formula I, or a pharmaceutically-acceptable salt thereof, according to claim 1 but without the proviso that the group of formula Ic so formed is not a purine ring and including the compounds :-
1-(6,7-dimethoxyquinazolin-4-yl)-3-phenylurea,
1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-phenylurea,
1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-bromophenyl)urea,
1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-methoxyphenyl)urea.
1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,
1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and
1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea.